

DETAILED ACTION

Status of Claims

Claims 1- 60 were originally filed on August 21, 2006.

The amendments filed on August 21, 2006, amended claims 6, 7, 9, 11, 13, 14, 16-19, 21, 24, 27-29, 33-36, 38, 39, 44-48, and 51 and canceled claims 54-60.

The amendments filed on January 20, 2012, amended claims 1, 38, 40-43, 45-48 and canceled claims 4, 17-37, 39, 44, and 51-53.

Claims 1-3, 5-16, 38, 40-43, and 45-50 are currently pending and under examination.

Election/Restrictions

Applicant's election without traverse of Group I (Claims 1-16 and 37-50) in the reply filed on April 28, 2011 is acknowledged.

Claims 17-36 and 51-53 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group, there being no allowable generic or linking claim.

Withdrawn Objection(s) and/or Rejection(s)

The objection to drawings because Figure 12, part c is labeled “FUG 12 c” is withdrawn in view of Applicants’ amendments filed on January 20, 2012.

The objection to the specification for not providing a description for Figure 12 c is withdrawn in view of Applicants’ amendments filed on January 20, 2012.

The objection to claim 4 is withdrawn in view of Applicants’ amendments filed on January 20, 2012.

The rejections for claims 1-16, 43, and 44 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention are withdrawn in view of Applicants’ amendments filed on January 20, 2012.

The rejection for claims 37, 38, 39, 45, and 48 under 35 U.S.C. 102(b) as being anticipated by Kim et al. (US 2003/0008413 A1; published January 2003) is withdrawn in view of Applicants’ amendments filed on January 20, 2012.

New Objection(s) and/or Rejection(s) Necessitated By Amendment

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 42 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 42 recites the limitation "the polyelectrolyte multilayer" in line 1. There is insufficient antecedent basis for this limitation in the claim because there is no polyelectrolyte multilayer present in claim 43 from which claim 42 depends

Claim 43 recites a "hydrogel support" in the preamble to which a plurality of molecules are directly attached, as well as a "solid support" in the body of the claim. Claim 43 is indefinite because it is unclear whether the hydrogel support is the same as the recited solid support or different. The indefiniteness of claims 43 is further exacerbated by claim 40 , which recites the embodiment wherein "the molecules of interest are attached directly or through a linking moiety to a silica-based support". Are the molecules attached directly to the silica-based support or are the molecules attached to a hydrogel wherein the hydrogel is immobilized on a solid support made of silica (silica-based) such as in the solid supported hydrogel array? If Applicants intend for the hydrogel to be immobilized to a solid support, Applicants are kindly directed to present claim 1, which utilizes the language "the hydrogel is immobilized to a solid support". If Applicants use the same language as in present claim 1 to clearly define the metes and bounds of the support

onto which the molecules of interest and hydrogel are immobilized, please note that when two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Maintained Objection(s) and/or Rejection(s)

Please note that the rejections have been modified necessitated by amendment.

Claim Rejections - 35 USC § 102

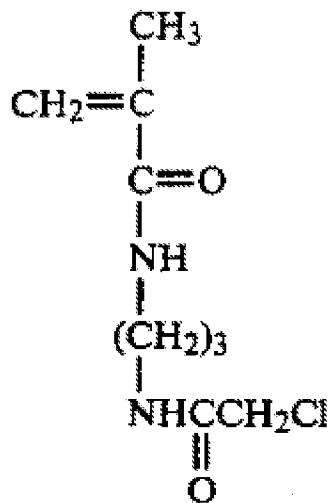
The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

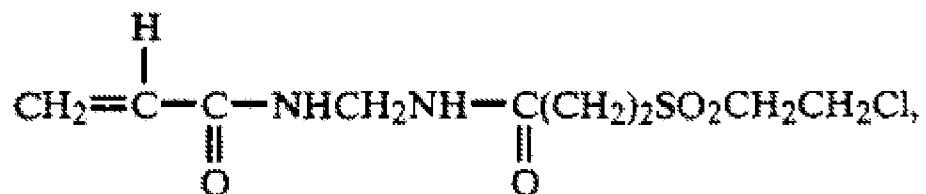
Claims 1, 2, 6-9, 11, and 14-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Ponticello et al. (US 5,212,253; May 1993; of record).

Regarding instant claim 1, Ponticello et al. disclose a method of polymerizing Poly[acrylamide-co-N-(3-chloroacteamidopropyl)methacrylamide] copolymer mixture between two glass plates (support; not covalently modified). The mixture comprises acrylamide (first comonomer) and N-(3-chloroacetamidopropyl)-methacrylamide (second comonomer) wherein N-(3-chloroacetamidopropyl)-methacrylamide is a functionalized acrylamide of the Formula II as disclosed in the instant claim 1 and is reproduced below;



wherein A is NH; B is (CH₂)₃ and C is a group for reaction NHC(=O)-CH₂-Cl (chloroacetamido) (Refer to the Specification Col. 11, lines 10-68; Col. 12, lines 1-19).

Furthermore, Ponticello et al. disclose co-polymerizing acrylamide with an acrylamide derivative such as N-[3-(2-chloroethylsulfonyl) propionamidomethyl] acrylamide (Formula I as disclosed in the instant; reproduced below)

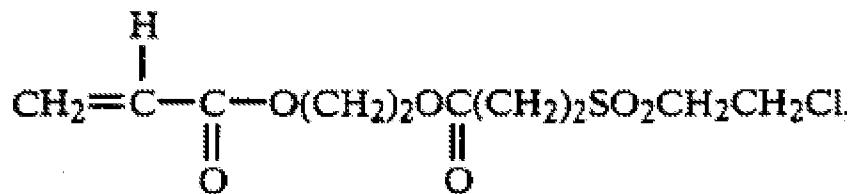


wherein A is NH, B is CH₂ and C is a group for reaction CH₂NHC(=O)-(CH₂)₂SO₂CH₂CH₂Cl or with N-[2-(ethoxycarbonylmethoxycarbonyl)ethyl]acrylamide (Formula I as disclosed in the instant claim 1; reproduced below)



wherein A is NH, B is $(\text{CH}_2)_2$ and C is a group for reaction $\text{COOCH}_2\text{COOC}_2\text{H}_5$

or with an acrylate derivative such as 2-[3-(2-chloroethylsulfonyl)propionyloxy]ethyl acrylate (Formula I as disclosed in the instant claim 1; reproduced below),

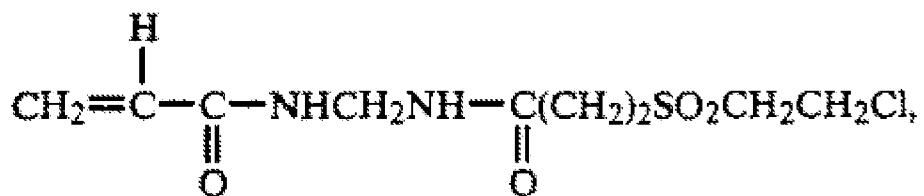


wherein A is O, B is $(\text{CH}_2)_2$ and C is a group for reaction $\text{OC}(\text{=O})-(\text{CH}_2)_2\text{SO}_2\text{CH}_2\text{CH}_2\text{Cl}$ (Refer to the Specification Col. 4, lines 18-45; Col. 8 lines 42-67).

Regarding instant claim 2, Ponticello et al. teach polymerizing a polymer solution between two glass plates (silica-based support) (Refer to the Specification Col. 9, lines 41-50; Col. 12, lines 12-15).

Regarding instant claim 6, Ponticello et al. disclose the comonomer is acrylamide (first comonomer) (Refer to the Specification Col. 8 lines 42-67; Col. 11, lines 10-54).

Regarding instant claims 7-9, Ponticello et al. disclose co-polymerizing acrylamide with an acrylamide derivative such as N-[3-(2-chloroethylsulfonyl)propionamidomethyl]acrylamide (Formula I)



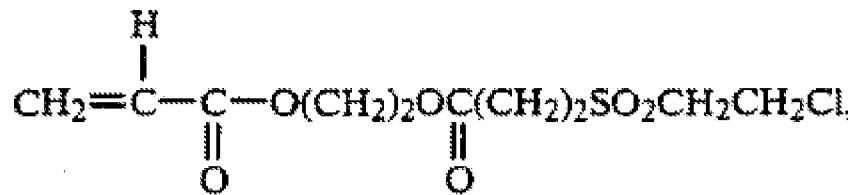
wherein A is NH, B is CH₂ and C is a group for reaction NHC(=O)-(CH₂)₂SO₂CH₂CH₂Cl

or N-[2-(ethoxycarbonylmethoxycarbonyl)ethyl]acrylamide (Formula I as disclosed in the instant claim 1)



wherein A is NH, B is $(\text{CH}_2)_2$ and C is a group for reaction $\text{COOCH}_2\text{COOC}_2\text{H}_5$

or with an acrylate derivative such as 2-[3-(2-chloroethylsulfonyl)propionyloxy]ethyl acrylate (Formula I as disclosed in the instant),



wherein A is O, B is $(\text{CH}_2)_2$ and C is a group for reaction $\text{OC}(\text{=O})-(\text{CH}_2)_2\text{SO}_2\text{CH}_2\text{CH}_2\text{Cl}$.

Furthermore, Ponticello disclose an acrylamide of formula (I) wherein A=NH and an acrylamide wherein B is C₂-C₁₀ alkylene biradical ((CH₂)₂, (CH₂)₃) (Refer to the Specification Col. 4, lines 18-45; Col. 8 lines 42-67; Col. 11, lines 10-54).

Regarding instant claim 11, Ponticello et al. disclose C is a haloacetamido (Refer to the Specification Col. 4, lines 18-45; Col. 8 lines 42-67; Col. 11, lines 10-54; Claim 1).

Regarding claims 14 and 15, Ponticello et al. disclose the mole ratio of acrylamide (first comonomer)/(3-chloroacetamidopropyl)-methacrylamide (second comonomer) is 96.5/3.5 (i.e. (3-chloroacetamidopropyl)-methacrylamide is present in the amount of 3.5% relative to the total molar quantity of total comonomers) which reads on the limitations in instant claims 14 and 15, of ≥ 1 mol% and ≥ 2 mol% relative to the total molar quantity of total comonomers (Refer to the Specification, Col. 13, lines 35-46).

Regarding claim 16, Ponticello disclose the method of polymerizing acrylamide N-(3-chloroacetamidopropyl)methacrylamide with no crosslinking agent or with dithiothreitol (no polyunsaturated crosslinking agent is present during polymerizing) (Refer to the Specification, Col. 11, lines 10-30 and Col. 12, lines 1-7).

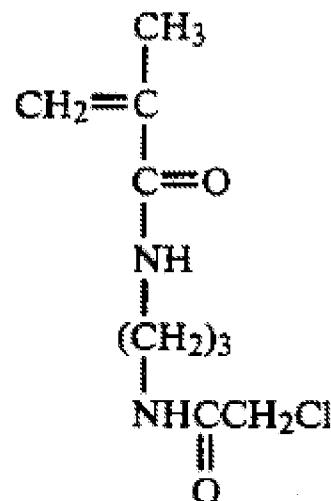
Therefore, the teachings of Ponticello et al. anticipate the presently claimed invention.

Response to Arguments

Applicant's arguments filed January 20, 2012 have been fully considered but they are not persuasive for the following reasons.

First, Applicants contend that Ponticello et al. do not teach the genus or species of compounds recited in claim 1. Applicants' arguments are not convincing since the teachings of

Ponticello et al. anticipate the presently claimed invention. Stated in the rejection set forth above, Ponticello et al. teach co-polymerizing acrylamide (first comonomer) and N-(3-chloroacetamidopropyl)-methacrylamide (second comonomer) wherein N-(3-chloroacetamidopropyl)-methacrylamide as well as other similar monomers that fall within the claimed genus of Formula I or Formula II. The examiner thanks the Applicant for pointing out the typographical error in the discussion of structure I in column 6 of Ponticello et al. in the previous Office action. The examiner agrees that L would be most analogous to -CONH(CH₂)₅- wherein k and n are 0 in the formula for L. However, the examiner disagrees with the Applicants contention that this analogous structure and genus recited in present claim 1 do not fit within the teachings of Ponticello et al. The teachings of Ponticello et al. do in fact fit within the genus and analogous structure of the presently claimed invention. For example, Ponticello et al. teach copolymerizing a first monomer of acrylamide with a second monomer wherein the monomer is N-(3-chloroacetamidopropyl)-methacrylamide.



has the below structure that fits within the genus of Formula II

wherein A is NH; B is $(CH_2)_3$ and C is a group for reaction $NHC(=O)-CH_2-Cl$ (chloroacetamido) (Refer to the Specification Col. 11, lines 10-68; Col. 12, lines 1-19). Furthermore, structure of L $-(R_3)_k-(COXR_4)_m-(NHCO)_n$ fits the analogous structure of $-CONH-(CH_2)_5$ because when k and n are 0, the structure of L is $COXR_4$ wherein X is NH and R^4 is a alkylene of 1 to 6 carbons and the group $(CH_2)_5$ is an alkylene of 5 carbons.

Second, Applicants contend that Ponticello et al. “do not describe polymerization on a solid support that has not been surface-modified”. Ponticello et al. describe the preparation of copolymers by a process described, for example, in Example 4 (Col 11, Lines 60-68 and Col. 12, Lines 1-19). Ponticello et al. do not explicitly state whether the glass supports are or are not surface modified and, accordingly one cannot ascertain whether the glass supports are surface modified or are not surface modified. The Office does not have the facilities and resources to provide the factual evidence needed in order to determine if all of the glass supports taught by Ponticello et al. correlate with the presently claimed solid support that has not been surface-modified. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the solid support that has not been surface-modified is different from the glass supports taught by the prior art and to establish the patentable differences. See *in re Best* 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray* 10 USPQ2d 1922(PTO Bd.Pat. App. & Int. 1989).

In addition, although Ponticello et al. is silent on the modification of the surface to which the copolymers are applied, Ponticello et al. anticipate the active method steps of present claim 1.

Based on this reasoning, it appears that Ponticello et al. describe the preparation of copolymers immobilized to a solid support that is not surface modified. *In re Best, Bolton, and Shaw* (195 USPQ 430) teaches the following: “Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See *In re Ludtke*, *supra* (169 USPQ 563).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

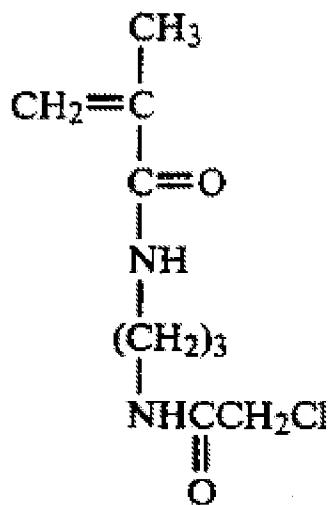
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

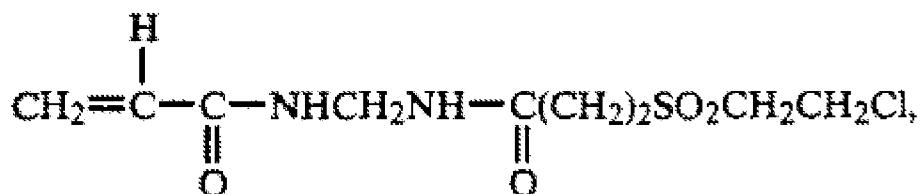
Claims 1-3 and 5-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ponticello et al. (US 5,212,253; May 1993; of record) in view of Leon et al. (US 2005/0064431 A1; filed September 2003; of record), and Patani et al. (“Bioisoterism: A Rational Approach in Drug Design, 1996”, Chemical Reviews, 96, 3147-3176; of record).

Regarding instant claim 1, Ponticello et al. teach a method of polymerizing Poly[acrylamide-co-N-(3-chloroacteamidopropyl)methacrylamide] copolymer mixture between two glass plates (support; not covalently modified). The mixture comprises acrylamide (first comonomer) and N-(3-chloroacetamidopropyl)-methacrylamide (second comonomer) wherein N-(3-chloroacetamidopropyl)-methacrylamide is a functionalized acrylamide of the Formula II as disclosed in the instant claim 1 and is reproduced below;



wherein A is NH; B is (CH₂)₃ and C is a group for reaction NHC(=O)-CH₂-Cl (chloroacetamido)
(Refer to the Specification Col. 11, lines 10-68; Col. 12, lines 1-19).

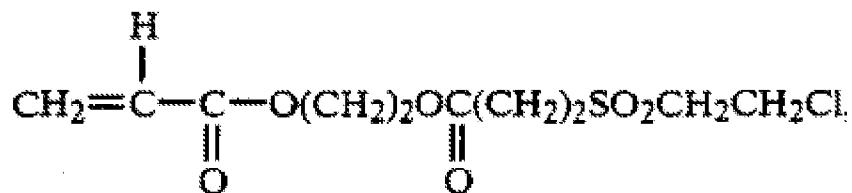
Furthermore, Ponticello et al. teach co-polymerizing acrylamide with an acrylamide derivative such as N-[3-(2-chloroethylsulfonyl) propionamidomethyl] acrylamide (Formula I as disclosed in the instant; reproduced below)



wherein A is NH, B is CH₂ and C is a group for reaction CH₂NHC(=O)-(CH₂)₂SO₂CH₂CH₂Cl , or with N-[2-(ethoxycarbonylmethoxycarbonyl)ethyl]acrylamide (Formula I as disclosed in the instant claim 1; reproduced below)



wherein A is NH, B is $(\text{CH}_2)_2$ and C is a group for reaction $\text{COOCH}_2\text{COOC}_2\text{H}_5$, or with an acrylate derivative such as 2-[3-(2-chloroethylsulfonyl)propionyloxy]ethyl acrylate (Formula I as disclosed in the instant claim 1; reproduced below),

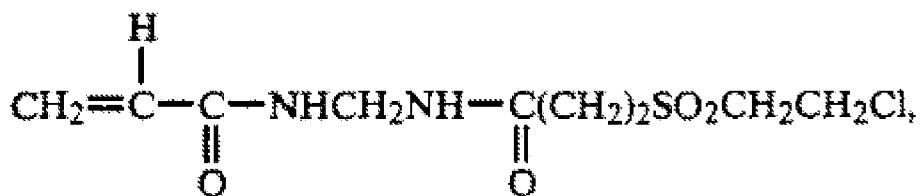


wherein A is O, B is $(\text{CH}_2)_2$ and C is a group for reaction $\text{OC}(\text{=O})-(\text{CH}_2)_2\text{SO}_2\text{CH}_2\text{CH}_2\text{Cl}$ (Refer to the Specification Col. 4, lines 18-45; Col. 8 lines 42-67).

Regarding instant claim 2, Ponticello et al. teach polymerizing a polymer solution between two glass (silica-based support) plates (Refer to the Specification Col. 9, lines 41-50; Col. 12, lines 12-15).

Regarding instant claim 6, Ponticello et al. teach the comonomer is acrylamide (first comonomer) (Refer to the Specification Col. 8 lines 42-67; Col. 11, lines 10-54.

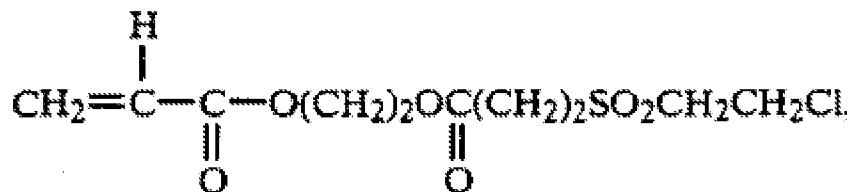
Regarding instant claims 7-9, Ponticello et al. teach co-polymerizing acrylamide with an acrylamide derivative such as N-[3-(2-chloroethylsulfonyl)propionamidomethyl]acrylamide (Formula I as disclosed in the instant claim 1)



wherein A is NH, B is CH₂ and C is a group for reaction CH₂NHC(=O)-(CH₂)₂SO₂CH₂CH₂Cl, or N-[2-(ethoxycarbonylmethoxycarbonyl)ethyl]acrylamide (Formula I as disclosed in the instant claim 1)



wherein A is NH, B is (CH₂)₂ and C is a group for reaction COOCH₂COOC₂H₅, or with an acrylate derivative such as 2-[3-(2-chloroethylsulfonyl)propionyloxy]ethyl acrylate (Formula I as disclosed in the instant),



wherein A is O, B is (CH₂)₂ and C is a group for reaction OC(=O)-(CH₂)₂SO₂CH₂CH₂Cl.

Furthermore, Ponticello teach an acrylamide of formula (I) wherein A=NH and an acrylamide wherein B is C₂-C₁₀ alkylene biradical ((CH₂)₂, (CH₂)₃) (Refer to the Specification Col. 4, lines 18-45; Col. 8 lines 42-67; Col. 11, lines 10-54).

Regarding instant claims 11 and 12, Ponticello et al. teach C is a haloacetamido (bromoacetamido) (Refer to the Specification Col. 4, lines 18-45; Col. 8 lines 42-67; Col. 11, lines 10-54; Claim 1).

Regarding instant claim 13, Ponticello et al. teach an acrylamide derivative with the following formula



wherein R^1 is a hydrogen or methyl, R^2 is a haloacetamido, and L is an $-(\text{R}_3)_k-(\text{COXR}_4)_m-$ $(\text{NHCO})_n-$ group where R_3 is arylene, R_4 is alkylene of 1 to 6 carbon atoms, X is $-\text{O}-$ or $-\text{NH}-$; and k, m, and n are each 0 or 1 provided that k is 0 when m is 1 and m is 0 when k is 1. Thus the acrylamide formula with the functional group options disclosed by Ponticello et al. read on N-(5-bromoacetamidopentyl) acrylamide wherein R^1 is a hydrogen, L is of the formula $-(\text{R}_3)_0-$ $(\text{COXR}_4)_1-(\text{NHCO})_0-$ group where k = n is 0, m is 1, X is NH, R_4 is an alkylene of 5 carbon atoms which read on $(\text{CH}_2)_5$, and R^2 is a haloacetamido which reads on bromoacetamido.

Regarding instant claims 14 and 15, Ponticello et al. teach the mole ratio of acrylamide (first comonomer)/(3-chloroacetamidopropyl)-methacrylamide (second comonomer) is 96.5/3.5 (i.e. (3-chloroacetamidopropyl)-methacrylamide is present in the amount of 3.5% relative to the total molar quantity of total comonomers) which reads on the limitations, in instant claims 14

and 15, of ≥ 1 mol% and ≥ 2 mol% relative to the total molar quantity of total comonomers (Refer to the Specification, Col. 13, lines 35-46).

Regarding instant claim 16, Ponticello teach the method of polymerizing acrylamide N-(3-chloroacetamidopropyl)methacrylamide with no crosslinking agent or with dithiothreitol (polyunsaturated crosslinker) (Refer to the Specification, Col. 11, lines 10-30 and Col. 12, lines 1-7).

Ponticello et al. do not explicitly teach fused silica (Claim 3), non-silica-based support (Claim 5), and Bromoacetamido (Claim 12 and 13).

Regarding instant claims 3 and 5, Leon et al. teach fused silica (silica based) and non-silica (i.e. plastics, metals, and semiconductors) as supports for microarrays comprised of copolymers (Refer to the Specification [0021, 0022]).

Regarding instant claims 12 and 13, Patani et al. teach bioisoterism wherein bioisosteres are defined to “include all atoms and molecules which fit the broadest definition for isosteres and have a similar type of biological activity” and are “compounds or groups that possess near-equal molecular shapes and volumes, approximately the same distribution of electrons, which exhibit similar properties” (Refer to Page 3148, Para(s) 4). For example, Cl is a bioisoster for Br (Refer to Table 3 and Table 16).

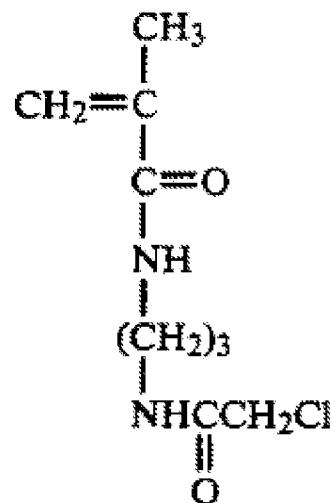
All of the claimed elements were known in the prior art and at the time of the invention, one of ordinary skill in the art would be motivated to combine the prior art reference teachings to arrive at the claimed invention. It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the Cl group in R² (chloroacetamido) taught by Ponticello et al. with Br taught by Patani et al.. One would be motivated to substitute Cl with Br to obtain bromoacetamido because Patani et al. clearly suggest that such a substitution would produce a compound with similar properties and one of ordinary skill in the art would have reasonably expected that a haloacetamido comprising Br would not change the properties of a compound significantly. Furthermore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Ponticello et al. and polymerize a mixture of acrylamide and an acrylamide derivative that contains a group for reaction with a compound of interest on a support consisting of fused silica or a non-silica based material such as plastic as an alternative to a glass support, as suggested by Leon et al. (Refer to the Specification [0021]). Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to polymerize a copolymer comprising a group for reaction with a compound of interest on a support glass, fused silica, and plastics. (Please see *KSR International Co. v. Teleflex Inc. (KSR)*, 550 USPQ2d 1385 (2007))

Response to Arguments

Applicant's arguments filed January 20, 2012 have been fully considered but they are not persuasive for the following reasons.

First, Applicants contend that Ponticello et al. do not teach the genus or species of compounds recited in claim 1. Applicants' arguments are not convincing since the teachings of Ponticello et al. in view of Leon et al. and Patani et al. render the method of preparing a hydrogel as presently claimed *prima facie* obvious. Stated in the rejection set forth above, Ponticello et al. teach co-polymerizing acrylamide (first comonomer) and N-(3-chloroacetamidopropyl)-methacrylamide (second comonomer) wherein N-(3-chloroacetamidopropyl)-methacrylamide as well as other similar monomers that fall within the claimed genus of Formula I or Formula II.

The examiner thanks the Applicant for pointing out the typographical error in the discussion of structure I in column 6 of Ponticello et al. in the previous Office action. The examiner agrees that L would be most analogous to -CONH(CH₂)₅- wherein k and n are 0 in the formula for L. However, the examiner disagrees with the Applicants contention that this analogous structure and genus recited in present claim 1 do not fit within the teachings of Ponticello et al.. The teachings of Ponticello et al. do in fact fit within the genus and analogous structure of the presently claimed invention. For example, Ponticello et al. teach copolymerizing a first monomer of acrylamide with a second monomer wherein the monomer is N-(3-chloroacetamidopropyl)-methacrylamide. N-(3-chloroacetamidopropyl)-methacrylamide has the



below structure that fits within the genus of Formula II , wherein

A is NH; B is (CH₂)₃ and C is a group for reaction NHC(=O)-CH₂-Cl (chloroacetamido) (Refer to the Specification Col. 11, lines 10-68; Col. 12, lines 1-19). Furthermore, structure of L (-(R₃)_k-(COXR₄)_m-(NHCO)_n) fits the analogous structure of -CONH-(CH₂)₅ because when k and n are 0, the structure of L is COXR₄ wherein X is NH and R⁴ is a alkylene of 1 to 6 carbons and the group (CH₂)₅ is an alkylene of 5 carbons.

Secondly, in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Claims 38, 40-43, and 45-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim et al. (US 2003/0008413 A1; published January 2003; of record) in

view of Ponticello et al. (US 5,212,253; May 1993; of record), Rubner et al. (US 2003/0157260 A1; published August 2003; of record), Mir (US 2004/0248144 A1; published December 2004; of record), and Adessi et al. (WO 00/18957; published April 2000; of record).

Regarding instant claims 43 and 48, Kim et al. teach a method comprising the step of applying polyelectrolyte films and coatings (polyelectrolyte) to a substrate surface (support) comprising attached biomolecules (immobilized biomolecules) for the production of high performance microarrays of biomolecules (molecular array comprising a plurality of molecules) (Refer to the Specification [0045 and 0080]).

Regarding instant claim 38, Kim et al. teach the molecules of interest are biomolecules (e.g. peptide, amino acid, proteins, nucleic acids) (Refer to the Specification [0001-0003, 0020-0029, 0045, 0052, 0072, 0075, 0079, 0080, and 0100]).

Regarding instant claim 45, Kim et al. teach the polyelectrolyte applied is polyacrylic acid (Refer to the Specification ([0016]).

Kim et al. do not explicitly teach molecules attach directly or through a linking moiety to a silica-based support (Claim 40), polyelectrolyte multilayers comprising polyacrylic acid and polyallylamine (Claims 42, and 46), a hydrogel obtained by a method comprising polymerizing a mixture of a first comonomer and second functionalized comonomer of formula (I) and (II) on a solid support that is not covalently surface-modified (Claim 43), polyacrylamide (Claim 41),

polyethylene glycol (Claim 47), single molecule array (Claim 49), and a clustered microarray (Claim 50).

Regarding instant claims 42, and 46, Rubner et al. teach polyelectrolyte multilayers comprising applying polyacrylic acid and polyallylamine hydrochloride (polyallylamine) to articles (e.g. cellular arrays or protein arrays), wherein biomolecules attached to the surface of the multilayers and the top layer is polyacrylic acid (surface to which the biomolecules are attached; polyallylamine applied followed by polyacrylic acid) (Refer to the Specification [0040 - 0043, 0051, 0052, 0079, 0092-0093]; Claims 1, 2, 4, 5, 7, 10, 11, 13, 14, 38, 39, 41, and 49).

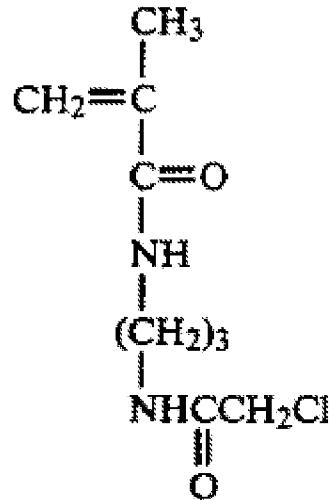
Regarding instant claim 40, Mir teaches the attachment of a plurality of molecules (e.g. nucleic acids such as DNA and analogues and derivative thereof; biomolecules) to a substrate covalently, non-covalently, via a layer of intermediate molecules to which the plurality of molecules bind, directly, or indirectly (Refer to the Specification [0148, 0156, 0165]).

Regarding instant claim 41, Mir teaches the molecules are immobilized on polyacrylamide substrate (Refer to the Specification [0174 and 0347]).

Regarding instant claim 47, Mir teaches coating the surface of the substrate with polyethylene glycol (Refer to the Specification [0165]).

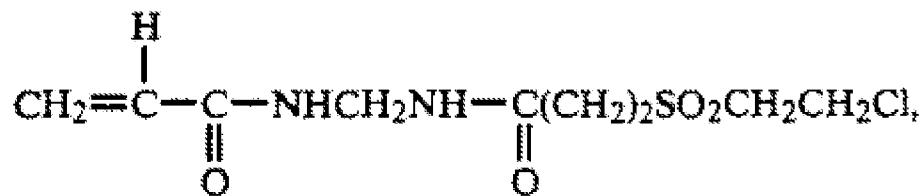
Regarding instant claims 48 and 49, Mir teaches a method comprising a single molecule array (Refer to the Specification [0043, 0128, 0170, 0171, 0172, 0175, 0182, 0288, 0459, 0480, 0507-0529, 0755-0794]).

Regarding instant claim 43, Ponticello et al. teach a method of polymerizing Poly[acrylamide-co-N-(3-chloroacteamidopropyl)methacrylamide] copolymer mixture between two glass plates (support; not covalently modified). The mixture comprises acrylamide (first comonomer) and N-(3-chloroacetamidopropyl)-methacrylamide (second comonomer) wherein N-(3-chloroacetamidopropyl)-methacrylamide is a functionalized acrylamide of the Formula II as disclosed in the instant claim 1 and is reproduced below;



wherein A is NH; B is (CH₂)₃ and C is a group for reaction NHC(=O)-CH₂-Cl (chloroacetamido) (Refer to the Specification Col. 11, lines 10-68; Col. 12, lines 1-19).

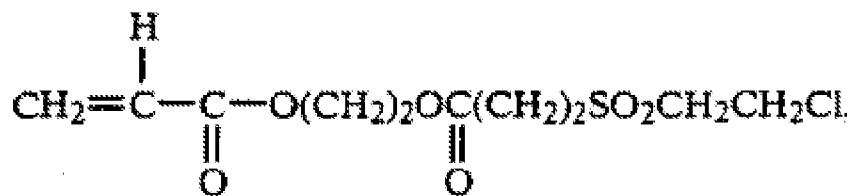
Furthermore, Ponticello et al. teach co-polymerizing acrylamide with an acrylamide derivative such as N-[3-(2-chloroethylsulfonyl) propionamidomethyl] acrylamide (Formula I as disclosed in the instant; reproduced below)



wherein A is NH, B is CH₂ and C is a group for reaction CH₂NHC(=O)-(CH₂)₂SO₂CH₂CH₂Cl, or with N-[2-(ethoxycarbonylmethoxycarbonyl)ethyl]acrylamide (Formula I as disclosed in the instant claim 1; reproduced below)



wherein A is NH, B is (CH₂)₂ and C is a group for reaction COOCH₂COOC₂H₅, or with an acrylate derivative such as 2-[3-(2-chloroethylsulfonyl)propionyloxy]ethyl acrylate (Formula I as disclosed in the instant claim 1; reproduced below),



wherein A is O, B is (CH₂)₂ and C is a group for reaction OC(=O)-(CH₂)₂SO₂CH₂CH₂Cl (Refer to the Specification Col. 4, lines 18-45; Col. 8 lines 42-67).

Regarding claim 50, Adessi et al. teach clustered microarrays (defined in the instant specification as “an array produced by solid-phase amplification of a target or template polynucleotide, wherein amplified copies of the target or template become covalently bound to the support during amplification”, Refer to Page 30, lines 21-35 in the instant specification) (Refer to the Specification Page 10, lines 7-36 and Page 11, lines 1-5; Figures 1 and 2 and corresponding captions).

All of the claimed elements were known in the prior art and at the time of the invention, one of ordinary skill in the art would be motivated to combine the prior art reference teachings to arrive at the claimed invention. It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a support comprising of polyallylamine and polyacrylic acid multilayers, wherein the top surface of the multilayers is polyacrylic acid. One would be motivated to use a support comprising polyelectrolyte multilayers because polyelectrolyte multilayers are bioinert as taught by Rubner et al. (Refer to the Specification [0007]) wherein nonspecific physiological responses are reduced. Moreover, one of ordinary skill would be motivated to have the top surface of the multilayer comprise polyacrylic acid because biomolecules can readily bind to the polyelectrolyte multilayers via the carboxylic group of polyacrylic acid. In addition, one of ordinary skill in the art would be motivated to apply polyethylene glycol (PEG) to the surface of a support (e.g. silica based support) because PEG is an inert chemical group that can be used to improve molecular binding of poorly binding molecules to some substrates providing a chemical interface between a solid surface and the molecules for molecular binding. Similarly, one of ordinary skill in the art would be motivated

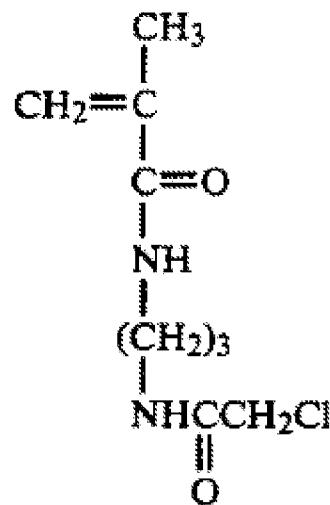
to use a polyacrylamide support because polyacrylamide is chemically inert. Furthermore, one of ordinary skill in the art would be motivated to use a copolymer comprising an acrylamide and a functionalized acrylamide/acrylate or methacrylate/methacrylamide monomer of formula I or II of the instant claims because the copolymers have chemical moieties (e.g. Chloroacetamido group) for immobilization of biomolecules such as DNA and as suggested by Ponticello et al., acrylamide monomers are more stable to hydrolysis and they polymerize more readily with other acrylamide monomers such as functionalized acrylamide/acrylate or methacrylate/methacrylamide (Refer to the Specification, Col. 8, lines 34-41).

Furthermore, one of ordinary skill in the art would be motivated to attach a plurality of molecules in a single molecule array because as taught by Mir, single molecule arrays have many advantages such as (1) can resolve complex samples, (2) can separate correct signals from erroneous, and (3) eliminates need for sample amplification (Refer to the Specification [0480 - 0488]). Similarly, one of ordinary skill in the art would be motivated to attach a plurality of molecules in a clustered microarray because solid phase nucleic acid amplification enable a large number of distinct nucleic acid sequences to be arrayed and amplified simultaneously at a high density as taught by Adessi et al. (Refer to the Specification Page 8, lines 25-33). Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to develop a method to modify molecular arrays (e.g. single molecule or clustered) that have various surfaces such as polyacrylamide or polyelectrolyte multilayers. (Please see *KSR International Co. v. Teleflex Inc. (KSR)*, 550 USPQ2d 1385 (2007))

Response to Arguments

Applicant's arguments filed January 20, 2012 have been fully considered but they are not persuasive for the following reasons.

First, Applicants contend that Ponticello et al. do not teach the genus or species of compounds recited in claim 1. Applicants' arguments are not convincing since the teachings of Kim et al. in view of Ponticello et al., Rubner et al., Mir, and Adessi et al. render the method of modifying a molecular array as presently claimed *prima facie* obvious. Stated in the rejection set forth above, Ponticello et al. teach co-polymerizing acrylamide (first comonomer) and N-(3-chloroacetamidopropyl)-methacrylamide (second comonomer) wherein N-(3-chloroacetamidopropyl)-methacrylamide as well as other similar monomers that fall within the claimed genus of Formula I or Formula II. The examiner thanks the Applicant for pointing out the typographical error in the discussion of structure I in column 6 of Ponticello et al. in the previous Office action. The examiner agrees that L would be most analogous to -CONH(CH₂)₅- wherein k and n are 0 in the formula for L. However, the examiner disagrees with the Applicants contention that this analogous structure and genus recited in present claim 1 do not fit within the teachings of Ponticello et al.... The teachings of Ponticello et al. do in fact fit within the genus and analogous structure of the presently claimed invention. For example, Ponticello et al. teach copolymerizing a first monomer of acrylamide with a second monomer wherein the monomer is N-(3-chloroacetamidopropyl)-methacrylamide. N-(3-chloroacetamidopropyl)-methacrylamide



has the below structure that fits within the genus of Formula II ,

wherein A is NH; B is $(CH_2)_3$ and C is a group for reaction $NHC(=O)-CH_2-Cl$ (chloroacetamido) (Refer to the Specification Col. 11, lines 10-68; Col. 12, lines 1-19). Furthermore, structure of L $(-R_3)_k-(COXR_4)_m-(NHCO)_n$ fits the analogous structure of $-CONH-(CH_2)_5$ because when k and n are 0, the structure of L is $COXR_4$ wherein X is NH and R^4 is a alkylene of 1 to 6 carbons and the group $(CH_2)_5$ is an alkylene of 5 carbons.

Secondly, in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Future Communications

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LIANKO GARYU whose telephone number is (571)270-7367. The examiner can normally be reached on Monday through Thursday - 8:00 a.m. to 5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Amber D. Steele/
Primary Examiner, Art Unit 1654

Lianko G Garyu
Examiner
Art Unit 1654